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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| EXAMINER | |
|---|---|
| ANGELL, JON E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1635 | 8 |

DATE MAILED: 08/15/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/987,687 | COFFEY ET AL. | |
| | Examiner | Art Unit | |
| | J. Eric Angell | 1635 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) 1-21 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-21 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 7
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other

**DETAILED**

Claims 1-21 are pending in the application.

***Claim Rejections - 35 USC § 102***

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection under 35 U.S.C. 102(b) as being anticipated by Lee et al. (WO 99/08692) is withdrawn in view of the amendment.

2. Claims 1-8 and 11-16 rejected under 35 U.S.C. 102(b) as being anticipated by Barber et al. (US Patent 5,662,896).

Barber teaches a method for delivering a virus to a solid tumor to reduce growth of the tumor, comprising administering an effective amount of virus to a subject bearing the tumor, wherein the virus is capable of selectively killing tumor cells, by a base administration selected from the group consisting of:

(a) delivering a composition comprising the virus to multiple sites inside the tumor; and

(b) delivering directly into the tumor a composition comprising the virus, wherein the volume of the composition is between about 10% and 100% of the volume of the tumor

(see for instance: abstract; column 11, lines 1-19; column 37, line 27 through column 38, line 5).

Specifically, Barber teaches, "For example, within one embodiment a small metastatic lesion may be located and the [retroviral] vector injected several times in several different locations within the body of the tumor" (emphasis added), thus indicating administration of at least 3 injections (because "several" indicates "greater than two but less than many", as defined in Merriam-Webster's Collegiate Dictionary, Tenth Edition, pg. 1073) on the same day which also encompasses an additional administration concurrent with the base administration (claims 14 and 16) (see column 11, lines 5-9). Barber also teaches the administration of the about one-tenth to two-tenths of a milliliter of a viral vector into tumors that are about 1-4$mm^3$ in volume in mice (see column 37, lines 38-42) and indicates, "Multiple injections of the vector are given to the tumor every two to three days", thus indicating additional administrations of the virus composition after the base administration (claims 14 and 15) (see column 37, lines 45-46). Regarding the delivery of the viral composition, it is noted that the instant claim encompasses delivering "between about 10% to about 100% of the volume of the tumor"(emphasis added). Claims 1 and 13 do not specifically limit the volume to between 10% and 100%, but to a volume that is only between "about" 10% and "about" 100% or the tumor. The volume of vector composition taught by Barber can be considered "about 100%" of the tumor volume, and therefore anticipates the instant claims. The volume taught by Barber would also be at least 50% of the volume of the tumor (claims 11 and 12).

Barber also teaches that the virus may be an influenza virus or an adenovirus (see column 10, lines 44-65).

***Claim Rejections - 35 USC § 103***

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

The rejection under 35 U.S.C. 103(a) as being unpatentable over Lorence et al. (WO 94/25627) is withdrawn in view of the amendment.

The rejection under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (U.S. Patent 6,110,461) is withdrawn in view of the amendment.

4. Claims 2-6 and 17-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barber et al. (US Patent 5,662,896) in view of Lee et al. (WO 99/08692).

Barber teaches a method for delivering a virus to a solid tumor to reduce growth of the tumor, comprising administering an effective amount of virus to a subject bearing the tumor, wherein the virus is capable of selectively killing tumor cells, by a base administration selected from the group consisting of:

(a) delivering a composition comprising the virus to multiple sites inside the tumor; and

(b) delivering directly into the tumor a composition comprising the virus, wherein the volume of the composition is between about 10% and 100% of the volume of the tumor (see for instance: abstract; column 11, lines 1-19; column 37, line 27 through column 38, line 5).

Specifically, Barber teaches, "For example, within one embodiment a small metastatic lesion may be located and the [retroviral] vector injected several times in several different locations within the body of the tumor", thus indicating multiple injections on the same day which also encompasses an additional administration concurrent with the base administration (claims 14 and 16) (see column 11, lines 5-9). Barber also teaches the administration of the about one-tenth to two-tenths of a milliliter of a viral vector into tumors that are about 1-4$mm^3$ in volume in mice (see column 37, lines 38-42) and indicates, "Multiple injections of the vector are given to the tumor every two to three days", thus indicating additional administrations of the virus composition after the base administration (claims 14 and 15) (see column 37, lines 45-46). Regarding the delivery of the viral composition, it is noted that the instant claim encompasses delivering "between about 10% to about 100% of the volume of the tumor"(emphasis added). Claims 1 and 13 do not specifically limit the volume to between 10% and 100%, but to a volume that is only between "about" 10% and "about" 100% or the tumor. The volume of vector composition taught by Barber can be considered "about 100%" of the tumor volume, and therefore anticipates the instant claims. The volume taught by Barber would also be at least 50% of the volume of the tumor (claims 11 and 12).

Barber does not teach that the virus can be a reovirus, a mammalian reovirus, a human reovirus, a serotype 3 human reovirus, or a Dearing strain serotype 3 human reovirus.

However, Lee teaches a method for delivering a reovirus serotype 3 Daring strain virus to a solid tumor to reduce growth of the tumor, comprising administering an effective amount of virus to a subject bearing the tumor, wherein the virus is capable of selectively killing tumor cells, by delivering a composition comprising the virus to multiple sites inside the tumor; and

(see for instance, abstract; p.3 lines 1-15; p.9, lines17-20; p.34, lines 9-17; Examples 9 and 10; and Claim 38).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the method taught by Barber such that the viral vector that is delivered into the tumor is a Dearing strain serotype 3 virus with a reasonable expectation of success.

The motivation to combine the references to create claimed invention is provided by Lee who teaches that the Dearing strain serotype 3 virus is another viral vector that can be injected into solid tumors for therapeutic purposes.

1. Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barber et al. (U.S. Patent 5,662,896).

Barber teaches a method for delivering a virus to a solid tumor to reduce growth of the tumor, comprising administering an effective amount of virus to a subject bearing the tumor, wherein the virus is capable of selectively killing tumor cells, by a base administration selected from the group consisting of:

(a) delivering a composition comprising the virus to multiple sites inside the tumor; and

(b) delivering directly into the tumor a composition comprising the virus, wherein the volume of the composition is between about 10% and 100% of the volume of the tumor (see for instance: abstract; column 11, lines 1-19; column 37, line 27 through column 38, line 5).

Specifically, Barber teaches, "For example, within one embodiment a small metastatic lesion may be located and the [retroviral] vector injected several times in several different locations within the body of the tumor", thus indicating multiple injections on the same day which also encompasses an additional administration concurrent with the base administration (claims 14 and 16) (see column 11, lines 5-9). Barber also teaches the administration of the about one-tenth to two-tenths of a milliliter of a viral vector into tumors that are about 1-4$mm^3$ in volume in mice (see column 37, lines 38-42) and indicates, "Multiple injections of the vector are given to the tumor every two to three days", thus indicating additional administrations of the virus composition after the base administration (claims 14 and 15) (see column 37, lines 45-46). Regarding the delivery of the viral composition, it is noted that the instant claim encompasses delivering "between about 10% to about 100% of the volume of the tumor"(emphasis added). Claims 1 and 13 do not specifically limit the volume to between 10% and 100%, but to a volume that is only between "about" 10% and "about" 100% or the tumor. The volume of vector composition taught by Barber can be considered "about 100%" of the tumor volume, and therefore anticipates the instant claims. The volume taught by Barber would also be at least 50% of the volume of the tumor (claims 11 and 12).

Barber does not teach that specifically teach that the virus is delivered to at leas 5 sites inside the tumor mass, or that the virus is delivered to at least one site per 0.25 cubic centimeters of the tumor.

However, it would have been prima facie obvious to perform routine optimization, as noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Here, the method of delivering a virus to multiple sites in a tumor on the same day is disclosed in the prior art (see Hu, as mentioned above). The specific number of injections, including the number per of injections per volume of the tumor is considered a matter of routine optimization. Routine optimization is not considered inventive and no evidence has been presented that the methods of delivering the vector, including volume and number of injections was other than routine, that the effects resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

***Response to Arguments***

2. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection.

***Conclusion***

5. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

JEFFREY FREDMAN
PRIMARY EXAMINER

J. Eric Angell
August 5, 2002